IJHS (Egypt) 2025; 3(4): 124-129

International Journal of Health Sciences (Egypt)

Journal homepage: https://ijhegy.journals.ekb.eg/

Original article

Evaluation of Leptin hormone and magnesium levels in recently diagnosed migraine patients

Ah Wael Abdallah Ibrahim *, Aliaa Mohamed Abd Elkhalik Ahmed

Neurology Department, Faculty of medicine, Zagazig University, Egypt.

ARTICLE INFO

Article history:
Received 25 July 2025
Received in revised form 31 August 2025
Accepted 20 November 2022

Keywords:
Leptin
Migraine
magensium.

ABSTRACT

Background: Migraine episodes are associated with multiple severe debilitating headaches. Several factors and triggers determine migraine pathogenesis. Adipocytokines and magnesium are substantially involved in migraine pathogenesis. **Objectives**: Assessment of leptin and magnesium levels in patients recently diagnosed with migraine. **Subjects and methods**: It was done at period from January 2023 to May 2024 at Zagazig University Hospitals, Egypt; 63 recently diagnosed patients with migraine were presented within this case - control study, the level of leptin was measured and magnesium and compared the results with 66 healthy individuals who did not have any headache, renal, or gastrointestinal disorders, and no intake of magnesium tablets nor medications interfering with leptin metabolism. **Results**: Recently diagnosed migraine patients had leptin levels significantly less than the control individuals (39.8 ± 20.7, 48.9 ± 23.6; P < .05). The average magnesium levels were 0.8±0.3 in Migrainers, whereas controls showed higher levels 1.9±0.2 (average normal value: 1.8 – 2.3 mg/dl) (p<.001). **Conclusions**: Recently Migrainers had lower leptin hormone values in between migraine episodes than that of healthy individuals. The magnesium measurements were lower significantly in migrainers than in healthy subjects, and this indicated that deficiency of magnesium involved in migraine pathophysiology and episodes.

Introduction

Migraine is a debilitating neurovascular condition marked by episodes of intense headaches associated with autonomic mainfestation. Its pathology was unknown exactly, however meningeal arteries vasodilatation and neurogenic inflammation were responsible for the painful sensation of migraine [1]. Additionally there is a strong relation between elevated likelihood of vascular disease among migraine patients [2-5], there is a considerable relationship between migraine with obesity. Obesity is contributing factor to the conversion of episodic attack into chronic condition [6]. There is still unclear relationship between function of adipocytokines and migraine in obese patients. Leptin is a hormone produced by adipocytes that controls dietary intake and

DOI: 10.21608/IJHEGY.2025.417412.1072
* *Corresponding author:* Wael Abdallah Ibrahim
E-mail address: waelabdallahneuro@gmail.com

maintenance of energy balance. Circulating levels of leptin hormones act on higher centers in the brain preventing obesity additionally the appetite is decreased [7]. Obesity and diabetes can result from deficiency of leptin or resistance [8]. Also, leptin exerts vascular action via its receptors which was found on endothelial cells. Vasoconstriction results from leptin administration for long period [9, 10]; however vasodilation occurs in acute infusion [11]. In both situations, the sympathetic nervous system can be enhanced by leptin signaling, and migraine is associated with the autonomic nervous system dysfunction [12]. According to WHO criteria, individuals with BMI above 30 kg/m2 are considered obese [13].

Magnesium, that vital second intracellular cation which is essential for multiple intracellular processes and serves a pivotal role in migraine pathogenesis [14]. There is significant effect of magnesium deficiency in cortical spreading depression, it affects platelet aggregation, the functions of serotonin receptors, and specific neurotransmitters release [15]. The cause of Magnesium deficiency in patients diagnosed with migraine can be due to defect in genes of magnesium reabsorption , loss of magnesium by kidneys, stress drains magnesium reserves, dietary deficient, or other factors [16].

This study, aimed to evaluate serum leptin and magnesium levels in recently diagnosed migraine patients.

Subjects and Methods:

A total of 63 participants recently diagnosed with migraine who presented at out-patients clinic in our Neurology Department, Zagazig University Hospitals, Egypt due to headache were included in this case-control study in the period between January 2023 and May 2024. Nearly all patients had migraine without aura, experiencing episodic attacks at a frequency of 1 to 6 times per month. To maintain study's validity, Patients with cardiovascular, renal, metabolic, psychiatric, or infectious diseases were excluded. Additionally, individuals taking medications that could infulence leptin metabolism or those on magnesium supplements were also excluded, as such diseases or treatment could affect serum magnesium concentration. All participants underwent neurological examination confirming normal. Migraine diagnosis followed (ICHD-II) criteria [17]. Data collected included the average number of monthly migraine attacks . Comprehensive assessment of blood pressure, anthropometric parameters (height, waist circumference [WC] and weight), fasting glucose and lipid profile. WC was determined at midpoint between iliac crest and the lowest rib while participants were lightly clothed. Body mass index was estimated using standard formulae, while fat mass, fat percentage and Lean mass were estimated using formula derived from the Quetelet index: [18] the equation applied was fat mass (kg)= ((A ×(weight)/(height)2 – B)) × (height)2; where A = 0.715 and B = 12.1 for males, and A = 0.713 and B = 9.74 for females. The control –group included 66 age- and gender- matched participants , with no previous history of migraine, no use of medications affecting leptin or magnesium levels, and free of renal or gastrointestinal disorders. All participants in both groups were of the same ethnicity and had similar socioeconomic backgrounds .Blood samples were obtained between 08:30 and 09:00 AM after overnight fast, using minimal tourniquet pressure. Fasting glucose and lipid profiles were measured immediately. For leptin and magensium, after centrifugation of blood samples at 3000 rpm for 10 minutes, the separated serum was preserved at -80°C in polypropylene tubes until testing. Magnesium, blood glucose, total cholesterol, triglycerides, HDL-C, and LDL-C levels were estimated by an Erba Chem-7 device. Serum leptin level was determined by ELISA technique using device named (Stat Fax-2100).

Statistical analysis:

Data were analyzed using IBM SPSS Statistics version 22(IBM Corp. released 2013). The Kolmogorov–Smirnov test was applied to verify normal data distribution. Depending on the variable type, comparisons between groups were performed using independent t-tests, chi-square, ANOVA, or Mann–Whitney U-test as appropriate. Univariate analysis adjusted leptin levels for fat mass. A p-value less than 0.05 considered significant.

Results:

Our research included 63 migraine participants (15 males [23.8%], average age: 37.5 ± 10.9 years; and 48 females [76.2%], average age: 36.5 ± 7.8 years) and 66 healthy control subjects (23 males [34.8%], average age: 35.6 ± 6.2 years; and 43 females [65.2%], average age: 33.4 ± 7.5 years). Age, BMI and WC

did not differ significantly between groups (P > 0.05). Table (1)

Compared to controls, individuals with migraine demonstrated significantly decreased leptin levels (39.8 ± 20.7 ng/mL vs. 48.9 ± 23.6 ng/mL; P < 0.05). Despite absence of significant difference in BMI and WC between two groups, migraine patients had significantly lower body fat percentages and fat mass (P < 0.001 for both). Additionally, fasting glucose levels were higher among migraineurs compared to controls, although still within the normal range (70–108 mg/dL vs. 56–101 mg/dL, respectively).

There were no significant differences between groups regarding mean arterial blood pressure or lipid profiles.

Serum magnesium were markedly lower in patient with migraine (0.8 ± 0.3 mg/dL) whereas levels in controls were (1.9 ± 0.2 mg/dL), with this difference being highly significant (P < 0.001). These values indicate that migraine patients had subnormal magnesium levels.

Correlation analysis revealed that leptin levels in the migraine group were positively associated with age, BMI, waist circumference, fat mass, and fat percentage (P < 0.05 for all) (Table 2). Logistic regression analysis revealed that fat mass independently predicted leptin levels (P < 0.05; β = 0.273; 95% CI: 0.06–0.764). When adjusted for fat mass, the disparity in level of leptin between migraine cases and controls disappeared. Additionally, headache frequency showed no association with either leptin concentration or fat mass (P > 0.05).

Table 1: Comparison of Clinical and Biochemical Parameters between Groups.

	Migraine group (n = 63)	**Control group (n = 66)**	***P***
Male/female	15/48	23/43	NS
Age (years) Males Females	 37.5 ± 10.9 36.5 ± 7.8	 35.6 ± 6.2 33.4 ± 7.5	 NS NS
BMI (kg/m2)	26.3 ± 5.8	26.6 ± 4.9	NS
WC (cm)	84.9 ± 11.4	84.6 ± 13.8	NS
SBP (mmHg)	118.6 ± 13.4	115.3 ± 14.9	NS
DBP (mmHg)	79.3 ± 12.3	76.6 ± 12.7	NS
Fasting glucose (mg/dL)	88.4 ± 8.7	81.9 ± 11.4	<.05
Total cholesterol (mg/dL)	186.3 ± 37.7	178.9 ± 36.9	NS
Triglyceride (mg/dL)	137.4 ± 126.9	104.5 ± 63.7	NS
LDL-C (mg/dL)	116 ± 33	107.8 ± 32.4	NS
HDL-C (mg/dL)	52.2 ± 12.3	47.4 ± 14.8	NS
Leptin (ng/mL)	39.8 ± 20.7	48.9 ± 23.6	<.05
Fat percentage (%)	28 ± 8	34 ± 6	<.001
Fat mass (kg)	19.8 ± 8.4	25.9 ± 9.4	<.001
Lean mass (kg)	44.8 ± 7.4	45.6 ± 8.5	NS
Mg (mg/dL)	0.8±0.3	1.9±0.2	<.001

BMI = body mass index; DBP = diastolic blood pressure; HDL-C = high density lipoprotein-cholesterol; LDL-C = low density lipoprotein-cholesterol; NS = non-significant; SBP = systolic blood pressure; WC = waist circumference; Mg = magnesium.

Table 2: Correlation between Leptin levels and Anthropometric Measures in Migraineurs.

	Leptin	
	r	***p***
Age	0.24	<.05
BMI	0.423	<.001
WC	0.278	<.05
Fat percentage	0.416	<.001
Fat mass	0.297	<.05
Lean mass	-0.289	<.05

BMI = body mass index; WC = waist circumference.

Discussion:

Migraine is a multifactorial disorder influenced by a variety of physiological, emotional, and environmental determinants. Over the past few years, particular attention has been given to the roles of leptin and magnesium in both the development and prevention of migraine episodes [19, 20].

In this study, we observed that both serum leptin levels and body fat mass were lower in migraine cases relative to healthy individuals. Leptin is produced by adipose tissue, and its plasma level typically reflects the total amount of stored fat. In general, individuals with higher fat mass exhibit elevated leptin levels. However, in obesity, the expected appetite-suppressing effects of high leptin levels are diminished due to leptin resistance [21].

Although the exact relationship between leptin and migraine pathogenesis remains unclear, several researches has shown that obese individuals may not have a higher incidence of migraine compared to standard body weight individuals, but they may experience more frequent attacks [21-23]. This implies that adipocytokines, such as leptin and adiponectin, could be involved in inflammatory processes relevant to migraine [24]. Adipose tissue also releases pro-inflammatory cytokines, including interleukin-6, tumor necrosis factor-alpha and calcitonin gene-related peptide which have been reported to rise during migraine attacks [19, 21]. However, in our study, these inflammatory markers were not assessed, so no definitive conclusions can be drawn about the role of leptin in migraine-associated inflammation.

Leptin is known to stimulate the sympathetic nervous system via hypothalamic activation [21]. In contrast, low leptin levels are typically associated with reduced sympathetic tone. Previous studies have demonstrated that migraineurs exhibit decreased sympathetic nervous system activity during interictal (headache-free) periods, which is evidenced by reduced plasma norepinephrine levels [12, 25]. The lower leptin concentrations observed in our migraine patients—measured during headache-free intervals—may reflect this baseline sympathetic underactivity, supporting the hypothesis that autonomic dysfunction contributes to migraine pathophysiology.

Magnesium is essential for proper nervous system function and contributes to multiple mechanisms linked to migraine, including neuroinflammation suppression, calcium channel blockade, NMDA receptor modulation, and regulation of serotonin activity and vascular tone [15].

The significant magnesium deficiency observed in our migraine group aligns with previous studies, reinforcing the theory that low magnesium levels contribute to migraine development and attack frequency [20, 26, 27, 28].

Furthermore, recent clinical trials have investigated the use of magnesium—alone or in combination with other medications as a preventive strategy for migraine. These findings support the therapeutic potential of magnesium supplementation in reducing the frequency and severity of migraine attacks [29, 30].

Conclusions and recommendations:

Our results indicate that individuals with recent migraine diagnosis migraine exhibit significantly lower serum leptin levels during headache-free phases, along with reduced fat mass compared to healthy controls. This suggests a potential link between leptin deficiency and migraine pathogenesis, possibly mediated through altered sympathetic nervous system activity or impaired energy regulation.

Moreover, serum magnesium concentrations were notably reduced in migraine cases than in the control group, underscoring the role of magnesium deficiency in triggering or exacerbating migraine episodes. These observations are consistent with existing literature and reinforce the involvement of both leptin and magnesium in migraine physiology. Thus, we recommend use of magnesium and leptin hormone as a future prophylactic therapeutic target in migraine patients.

Conflict of Interest:

There are no conflicts of interest.

Funding:

No funding sources.

References:

[1] Hargreaves R, Shepheard S. Pathophysiology of Migraine — New Insights. Can J Neurol Sci 1999; 26. https://doi.org/10.1017/S0317167100000147.

[2] Liew G, Wang JJ, Mitchell P. Migraine and coronary heart disease mortality: A prospective cohort study. Cephalalgia 2007;

27. https://doi.org/10.1111/j.1468-2982.2007.01298.x.

[3] Agostoni E, Fumagalli L, Santoro P, Ferrarese C. Migraine and stroke. Neurol Sci 2004; 25. https://doi.org/10.1007/s10072-004-0268-6.

[4] Kurth T, Gaziano JM, Cook NR, Bubes V, Logroscino G, Diener HC, et al. Migraine and risk of cardiovascular disease in men. Arch Intern Med 2007; 167. https://doi.org/10.1001/archinte.167.8.795.

[5] Scher AI, Terwindt GM, Picavet HSJ, Verschuren WMM, Ferrari MD, Launer LJ. Cardiovascular risk factors and migraine: The GEM population-based study. Neurology 2005; 64. https://doi.org/10.1212/01.WNL.0000151857.43225.49.

[6] Bigal ME, Lipton RB. Obesity is a risk factor for trans formed migraine but not chronic tension-type headache. Neurology 2006; 67. https://doi.org/10.1212/01.wnl.0000225052.35019.f9.

[7] Clément K, Vaisse C, Lahlou N, Cabrol S, Pelloux V, Cassuto D, et al. A mutation in the human leptin receptor gene causes obesity and pituitary dysfunction. Nature 1998; 392. https://doi.org/10.1038/32911.

[8] McGown C, Birerdinc A, Younossi ZM. Adipose tissue as an endocrine organ. Clin Liver Dis 2014; 18. https://doi.org/10.1016/j.cld.2013.09.012.

[9] Shek EW, Brands MW, Hall JE. Chronic Leptin Infusion Increases Arterial Pressure. Hypertension 1998; 31. https://doi.org/10.1161/01.HYP.31.1.409.

[10] Dunbar JC, Hu Y, Lu H. Intracerebroventricular leptin increases lumbar and renal sympathetic nerve activity and blood pressure in normal rats. Diabetes 1997; 46. https://doi.org/10.2337/diabetes.46.12.2040.

[11] Haynes WG, Morgan DA, Walsh SA, Mark AL, Sivitz WI. Receptor-mediated regional sympathetic nerve activation by leptin. J Clin Invest 1997; 100. https://doi.org/10.1172/JCI119532.

[12] Peroutka SJ. Migraine: A Chronic Sympathetic Nervous System Disorder. Headache 2004; 44. https://doi.org/10.1111/j.1526-4610.2004.04011.x.

[13] Cawley J. An economy of scales: A selective review of obesity's economic causes, consequences, and solutions. J Health Econ 2015; 43. https://doi.org/10.1016/j.jhealeco.2015.03.001.

[14] Taylor FR. Nutraceuticals and headache: The biological basis. Headache 2011; 51. https://doi.org/10.1111/j.1526-4610.2011.01847.x.

[15] Özturan A, Şanlıer N, Coşkun Ö. The Relationship Between Migraine and Nutrition. Turkish J Neurol 2016; 22. https://doi.org/10.4274/tnd.37132.

[16] Mauskop A, Varughese J. Why all migraine patients should be treated with magnesium. J Neural Transm 2012; 119. https://doi.org/10.1007/s00702-012-0790-2.

[17] Olesen J, Steiner TJ. The international classification of headache disorders, 2nd edn (ICDH-II). J Neurol Neurosurg Psychiatry 2004;75. https://doi.org/10.1136/jnnp.2003.031286.

[18] Garrow JS, Webster J. Quetelet's index (W/H2) as a measure of fatness. Int J Obes 1985; 9.

[19] Domínguez C, Vieites-Prado A, Pérez-Mato M, Sobrino T, Rodríguez-Osorio X, López A, et al. Role of adipocytokines in the pathophysiology of migraine: A cross-sectional study. Cephalalgia 2018;38. https://doi.org/10.1177/0333102417720213.

[20] Domitrz I, Cegielska J. Magnesium as an Important Factor in the Pathogenesis and Treatment of Migraine—From Theory to Practice. Nutrients 2022;14. https://doi.org/10.3390/nu14051089.

[21] Pan WW, Myers MG. Leptin and the maintenance of elevated body weight. Nat Rev Neurosci 2018;19. https://doi.org/10.1038/nrn.2017.168.

[22] Scher AI, Stewart WF, Ricci JA, Lipton RB. Factors associated with the onset and remission of chronic daily headache in a population-based study. Pain 2003;106. https://doi.org/10.1016/S0304-3959(03)00293-8.

[23] Bigal ME, Liberman JN, Lipton RB. Obesity and migraine: A population study. Neurology 2006;66. https://doi.org/10.1212/01.wnl.0000197218.05284.82.

[24] Peterlin BL, Sacco S, Bernecker C, Scher AI. Adipokines and Migraine: A Systematic Review. Headache 2016;56. https://doi.org/10.1111/head.12788.

[25] Martinez F, Castillo J, Pardo J, Lema M, Noya M. Catecholamine levels in plasma and CSF in migraine. J Neurol Neurosurg Psychiatry 1993;56. https://doi.org/10.1136/jnnp.56.10.1119.

[26] Slavin M, Li H, Khatri M, Frankenfeld C. Dietary magnesium and migraine in adults: A cross-sectional analysis of the National Health and Nutrition Examination Survey 2001–2004. Headache 2021;61. https://doi.org/10.1111/head.14065.

[27] Karim MR, Bhattacharjee M, Islam MS, Banerjee S, Hossain S, Hossain MI, et al. Relation between Serum Magnesium Level and Migraine. Mymensingh Med J 2021; 30.

[28] Assarzadegan F, Asgarzadeh S, Hatamabadi HR, Shahrami A, Tabatabaey A, Asgarzadeh M. Serum concentration of magnesium as an independent risk factor in migraine attacks. Int Clin Psychopharmacol 2016; 31. https://doi.org/10.1097/yic.0000000000000130.

[29] Gallelli L, Avenoso T, Falcone D, Palleria C, Peltrone F, Esposito M, et al. Effects of acetaminophen and ibuprofen in children with migraine receiving preventive treatment with magnesium. Headache 2014; 54. https://doi.org/10.1111/head.12162.

[30] Khani S, Hejazi SA, Yaghoubi M, Sharifipour E. Comparative study of magnesium, sodium valproate, and concurrent magnesium-sodium valproate therapy in the prevention of migraine headaches: a randomized controlled double-blind trial. J Headache Pain 2021; 22. https://doi.org/10.1186/s10194-021-01234-6.

Ibrahim W, Ahmed A. Evaluation of leptin hormone and magnesium levels in recently diagnosed migraine patients. International Journal of Health Sciences. IJHS (Egypt) 2025; 3(4): 124-129.